



COPY

SEQUENCE LISTING

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<120> CONJUGATES COMPRISING HUMAN IL-18 AND
SUBSTITUTION MUTANTS THEREOF

<130> PU60053

<140> 10/823,964

<141> 2004-04-14

<150> 60/462,947

<151> 2003-04-15

<160> 28

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<212> PRT

<213> Homo sapiens

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		20					25					30			
Met	Thr	Asp	Ser	Asp	Cys	Arg	Asp	Asn	Ala	Pro	Arg	Thr	Ile	Phe	Ile
		35				40						45			
Ile	Ser	Met	Tyr	Lys	Asp	Ser	Gln	Pro	Arg	Gly	Met	Ala	Val	Thr	Ile
	50				55					60					
Ser	Val	Lys	Cys	Glu	Lys	Ile	Ser	Thr	Leu	Ser	Cys	Glu	Asn	Lys	Ile
65				70					75					80	
Ile	Ser	Phe	Lys	Glu	Met	Asn	Pro	Pro	Asp	Asn	Ile	Lys	Asp	Thr	Lys
		85						90						95	
Ser	Asp	Ile	Ile	Phe	Phe	Gln	Arg	Ser	Val	Pro	Gly	His	Asp	Asn	Lys
		100						105					110		
Met	Gln	Phe	Glu	Ser	Ser	Ser	Tyr	Glu	Gly	Tyr	Phe	Leu	Ala	Cys	Glu
		115					120					125			
Lys	Glu	Arg	Asp	Leu	Phe	Lys	Leu	Ile	Leu	Lys	Lys	Glu	Asp	Glu	Leu
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Gly	Asp	Arg	Ser	Ile	Met	Phe	Thr	Val	Gln	Asn	Glu	Asp			
145				150						155					

<210> 2

<211> 157

<212> PRT

<213> Mus musculus

<400> 2

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Asp	Gln	Val	Leu	Phe	Val	Asp	Lys	Arg	Gln	Pro	Val	Phe	Glu	Asp	Met
		20						25					30		
Thr	Asp	Ile	Asp	Gln	Ser	Ala	Ser	Glu	Pro	Gln	Thr	Arg	Leu	Ile	Ile
	35						40					45			
Tyr	Met	Tyr	Lys	Asp	Ser	Glu	Val	Arg	Gly	Leu	Ala	Val	Thr	Leu	Ser
	50					55					60				
Val	Lys	Asp	Ser	Lys	Met	Ser	Thr	Leu	Ser	Cys	Lys	Asn	Lys	Ile	Ile
65					70					75					80
Ser	Phe	Glu	Glu	Met	Asp	Pro	Pro	Glu	Asn	Ile	Asp	Asp	Ile	Gln	Ser
			85						90					95	
Asp	Leu	Ile	Phe	Phe	Gln	Lys	Arg	Val	Pro	Gly	His	Asn	Lys	Met	Glu
			100					105						110	
Phe	Glu	Ser	Ser	Leu	Tyr	Glu	Gly	His	Phe	Leu	Ala	Cys	Gln	Lys	Glu
		115					120					125			
Asp	Asp	Ala	Phe	Lys	Leu	Ile	Leu	Lys	Lys	Lys	Asp	Glu	Asn	Gly	Asp
	130					135					140				
Lys	Ser	Val	Met	Phe	Thr	Leu	Thr	Asn	Leu	His	Gln	Ser			
145					150					155					

<210> 3

<211> 203

<212> PRT

<213> Homo sapiens

<400> 3

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Glu	Asp	Asn	Cys	Ile	Asn	Phe	Val	Ala	Met	Lys	Phe	Ile	Asp	Asn	Thr
		20						25					30		
Leu	Tyr	Phe	Ile	Ala	Glu	Asp	Asp	Glu	Asn	Leu	Glu	Ser	Asp	Tyr	Phe
	35						40					45			
Gly	Lys	Leu	Glu	Ser	Lys	Leu	Ser	Val	Ile	Arg	Asn	Leu	Asn	Asp	Gln
	50					55					60				
Val	Leu	Phe	Ile	Asp	Gln	Gly	Asn	Arg	Pro	Leu	Phe	Glu	Asp	Met	Thr
65					70					75					80
Asp	Ser	Asp	Cys	Arg	Asp	Asn	Ala	Pro	Arg	Thr	Ile	Phe	Ile	Ile	Ser
			85						90					95	
Met	Tyr	Lys	Asp	Ser	Gln	Pro	Arg	Gly	Met	Ala	Val	Thr	Ile	Ser	Val
			100					105						110	
Lys	Cys	Glu	Lys	Ile	Ser	Thr	Leu	Ser	Cys	Glu	Asn	Lys	Ile	Ile	Ser
		115					120					125			
Phe	Lys	Glu	Met	Asn	Pro	Pro	Asp	Asn	Ile	Lys	Asp	Thr	Lys	Ser	Asp
	130					135					140				
Ile	Ile	Phe	Phe	Gln	Arg	Ser	Val	Pro	Gly	His	Asp	Asn	Lys	Met	Gln
145					150					155					160
Phe	Glu	Ser	Ser	Ser	Tyr	Glu	Gly	Tyr	Phe	Leu	Ala	Cys	Glu	Lys	Glu
				165					170					175	
Arg	Asp	Leu	Phe	Lys	Leu	Ile	Leu	Lys	Lys	Glu	Asp	Glu	Leu	Gly	Asp
			180						185					190	

Arg Ser Ile Met Phe Thr Val Gln Asn Glu Asp
195 200

<210> 4
<211> 157
<212> PRT
<213> Homo sapiens

<220>
<223> Whereby the Cysteine at position 38 of this human IL-18
sequence has been replaced with Serine.

<400> 4
Tyr Phe Gly Lys Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn
1 5 10 15
Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp
20 25 30
Met Thr Asp Ser Asp Ser Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile
35 40 45
Ile Ser Met Tyr Lys Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile
50 55 60
Ser Val Lys Cys Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile
65 70 75 80
Ile Ser Phe Lys Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys
85 90 95
Ser Asp Ile Ile Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys
100 105 110
Met Gln Phe Glu Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu
115 120 125
Lys Glu Arg Asp Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Leu
130 135 140
Gly Asp Arg Ser Ile Met Phe Thr Val Gln Asn Glu Asp
145 150 155

<210> 5
<211> 157
<212> PRT
<213> Homo sapiens

<220>
<223> Whereby the Cysteine at position 38 of this human IL-18
sequence has been replaced with Serine, the Cysteine at
position 68 has been replaced with Aspartic acid, and the
Asparagine at position 78 has been replaced with Cysteine.

<400> 5
Tyr Phe Gly Lys Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn
1 5 10 15
Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp
20 25 30
Met Thr Asp Ser Asp Ser Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile
35 40 45
Ile Ser Met Tyr Lys Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile
50 55 60

Ser	Val	Lys	Asp	Glu	Lys	Ile	Ser	Thr	Leu	Ser	Cys	Glu	Cys	Lys	Ile
65					70					75					80
Ile	Ser	Phe	Lys	Glu	Met	Asn	Pro	Pro	Asp	Asn	Ile	Lys	Asp	Thr	Lys
			85						90					95	
Ser	Asp	Ile	Ile	Phe	Phe	Gln	Arg	Ser	Val	Pro	Gly	His	Asp	Asn	Lys
			100					105					110		
Met	Gln	Phe	Glu	Ser	Ser	Ser	Tyr	Glu	Gly	Tyr	Phe	Leu	Ala	Cys	Glu
		115					120					125			
Lys	Glu	Arg	Asp	Leu	Phe	Lys	Leu	Ile	Leu	Lys	Lys	Glu	Asp	Glu	Leu
	130					135					140				
Gly	Asp	Arg	Ser	Ile	Met	Phe	Thr	Val	Gln	Asn	Glu	Asp			
145					150					155					

<210> 6
 <211> 157
 <212> PRT
 <213> Homo sapiens

<220>
 <223> Whereby the Cysteine at position 38 of thi human IL-18 sequence has been replaced with Serine, the Cysteine at position 68 has been replaced with Aspartic acid, and the Glutamic acid at position 121 has been replaced with Cysteine.

Tyr	Phe	Gly	Lys	Leu	Glu	Ser	Lys	Leu	Ser	Val	Ile	Arg	Asn	Leu	Asn
1				5					10					15	
Asp	Gln	Val	Leu	Phe	Ile	Asp	Gln	Gly	Asn	Arg	Pro	Leu	Phe	Glu	Asp
		20						25				30			
Met	Thr	Asp	Ser	Asp	Ser	Arg	Asp	Asn	Ala	Pro	Arg	Thr	Ile	Phe	Ile
		35				40					45				
Ile	Ser	Met	Tyr	Lys	Asp	Ser	Gln	Pro	Arg	Gly	Met	Ala	Val	Thr	Ile
	50				55					60					
Ser	Val	Lys	Asp	Glu	Lys	Ile	Ser	Thr	Leu	Ser	Cys	Glu	Asn	Lys	Ile
65					70					75					80
Ile	Ser	Phe	Lys	Glu	Met	Asn	Pro	Pro	Asp	Asn	Ile	Lys	Asp	Thr	Lys
			85						90					95	
Ser	Asp	Ile	Ile	Phe	Phe	Gln	Arg	Ser	Val	Pro	Gly	His	Asp	Asn	Lys
			100					105					110		
Met	Gln	Phe	Glu	Ser	Ser	Ser	Tyr	Cys	Gly	Tyr	Phe	Leu	Ala	Cys	Glu
		115					120					125			
Lys	Glu	Arg	Asp	Leu	Phe	Lys	Leu	Ile	Leu	Lys	Lys	Glu	Asp	Glu	Leu
	130					135					140				
Gly	Asp	Arg	Ser	Ile	Met	Phe	Thr	Val	Gln	Asn	Glu	Asp			
145					150					155					

<210> 7
 <211> 157
 <212> PRT
 <213> Homo sapeins

<220>
 <223> Whereby the Cysteine at position 38 of this human IL-18 sequence has been replaced with Serine, the Cysteine at position 68 has been replaced with Aspartic acid, and the Leucine at position 144

has been replaced with Cysteine.

<400> 7

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Tyr Phe Gly Lys Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn
 1           5           10           15
Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp
          20           25           30
Met Thr Asp Ser Asp Ser Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile
          35           40           45
Ile Ser Met Tyr Lys Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile
          50           55           60
Ser Val Lys Asp Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile
65          70           75           80
Ile Ser Phe Lys Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys
          85           90           95
Ser Asp Ile Ile Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys
          100          105          110
Met Gln Phe Glu Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu
          115          120          125
Lys Glu Arg Asp Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Cys
130          135          140
Gly Asp Arg Ser Ile Met Phe Thr Val Gln Asn Glu Asp
145          150          155

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<210> 8

<211> 157

<212> PRT

<213> Homo sapiens

<220>

<223> Whereby the Cysteine at position 38 of the human IL-18 sequence has been replaced with Serine, the Cysteine at position 68 has been replaced with Aspartic acid, and Aspartic acid at position 157 has been replaced with Cysteine.

<400> 8

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Tyr Phe Gly Lys Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn
 1           5           10           15
Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp
          20           25           30
Met Thr Asp Ser Asp Ser Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile
          35           40           45
Ile Ser Met Tyr Lys Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile
          50           55           60
Ser Val Lys Asp Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile
65          70           75           80
Ile Ser Phe Lys Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys
          85           90           95
Ser Asp Ile Ile Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys
          100          105          110
Met Gln Phe Glu Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu
          115          120          125
Lys Glu Arg Asp Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Leu
130          135          140
Gly Asp Arg Ser Ile Met Phe Thr Val Gln Asn Glu Cys
145          150          155

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<210> 9
 <211> 157
 <212> PRT
 <213> Homo sapeins

<220>

<223> Whereby the Cysteine at position 38 of the human IL-18 sequence has been replaced with Serine, the Cysteine at position 68 has been replaced with Serine, and Leucine at position 144 has been replaced with Cysteine.

<400> 9

Tyr	Phe	Gly	Lys	Leu	Glu	Ser	Lys	Leu	Ser	Val	Ile	Arg	Asn	Leu	Asn
1				5				10						15	
Asp	Gln	Val	Leu	Phe	Ile	Asp	Gln	Gly	Asn	Arg	Pro	Leu	Phe	Glu	Asp
			20					25					30		
Met	Thr	Asp	Ser	Asp	Ser	Arg	Asp	Asn	Ala	Pro	Arg	Thr	Ile	Phe	Ile
			35					40					45		
Ile	Ser	Met	Tyr	Lys	Asp	Ser	Gln	Pro	Arg	Gly	Met	Ala	Val	Thr	Ile
			50				55				60				
Ser	Val	Lys	Ser	Glu	Lys	Ile	Ser	Thr	Leu	Ser	Cys	Glu	Asn	Lys	Ile
65					70				75					80	
Ile	Ser	Phe	Lys	Glu	Met	Asn	Pro	Pro	Asp	Asn	Ile	Lys	Asp	Thr	Lys
				85					90					95	
Ser	Asp	Ile	Ile	Phe	Phe	Gln	Arg	Ser	Val	Pro	Gly	His	Asp	Asn	Lys
				100					105					110	
Met	Gln	Phe	Glu	Ser	Ser	Ser	Tyr	Glu	Gly	Tyr	Phe	Leu	Ala	Cys	Glu
			115				120					125			
Lys	Glu	Arg	Asp	Leu	Phe	Lys	Leu	Ile	Leu	Lys	Lys	Glu	Asp	Glu	Cys
			130				135					140			
Gly	Asp	Arg	Ser	Ile	Met	Phe	Thr	Val	Gln	Asn	Glu	Asp			
145					150						155				

<210> 10
 <211> 157
 <212> PRT
 <213> Homo sapiens

<220>

<223> Whereby the Cysteine at position 38 of the human IL-18 sequence has been replaced with Serine, the Cysteine at position 68 has been replaced with Serine, and Aspartic acid at position 157 has been replaced with Cysteine.

<400> 10

Tyr	Phe	Gly	Lys	Leu	Glu	Ser	Lys	Leu	Ser	Val	Ile	Arg	Asn	Leu	Asn
1				5				10						15	
Asp	Gln	Val	Leu	Phe	Ile	Asp	Gln	Gly	Asn	Arg	Pro	Leu	Phe	Glu	Asp
			20					25					30		
Met	Thr	Asp	Ser	Asp	Ser	Arg	Asp	Asn	Ala	Pro	Arg	Thr	Ile	Phe	Ile
			35					40					45		

Ile	Ser	Met	Tyr	Lys	Asp	Ser	Gln	Pro	Arg	Gly	Met	Ala	Val	Thr	Ile
50						55					60				
Ser	Val	Lys	Ser	Glu	Lys	Ile	Ser	Thr	Leu	Ser	Cys	Glu	Asn	Lys	Ile
65					70					75					80
Ile	Ser	Phe	Lys	Glu	Met	Asn	Pro	Pro	Asp	Asn	Ile	Lys	Asp	Thr	Lys
			85						90					95	
Ser	Asp	Ile	Ile	Phe	Phe	Gln	Arg	Ser	Val	Pro	Gly	His	Asp	Asn	Lys
			100					105					110		
Met	Gln	Phe	Glu	Ser	Ser	Ser	Tyr	Glu	Gly	Tyr	Phe	Leu	Ala	Cys	Glu
		115					120					125			
Lys	Glu	Arg	Asp	Leu	Phe	Lys	Leu	Ile	Leu	Lys	Lys	Glu	Asp	Glu	Leu
	130					135					140				
Gly	Asp	Arg	Ser	Ile	Met	Phe	Thr	Val	Gln	Asn	Glu	Cys			
145					150					155					

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<220>
 <223> Tryptic peptides predicted for S-carboxymethylated
 wild type IL-18

<400> 11
 Tyr Phe Gly Lys
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<210> 12
 <211> 4
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Tryptic peptides predicted for S-carboxymethylated
 wild type IL-18

<400> 12
 Leu Glu Ser Lys
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<210> 13
 <211> 5
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Tryptic peptides predicted for S-carboxymethylated
 wild type IL-18

<400> 13

Leu Ser Val Ile Arg
1 5

<210> 14
<211> 26
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 14
Asn Leu Asn Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu
1 5 10 15
Phe Glu Asp Met Thr Asp Ser Asp Cys Arg
20 25

<210> 15
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 15
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1 5

<210> 16
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 16
Thr Ile Phe Ile Ile Ser Met Tyr Lys
1 5

<210> 17
<211> 5
<212> PRT
<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 17

Asp Ser Gln Pro Arg
1 5

<210> 18

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 18

Gly Met Ala Val Thr Ile Ser Val Lys
1 5

<210> 19

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 19

Ile Ser Thr Leu Ser Cys Glu Asn Lys
1 5

<210> 20

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 20

Ile Ile Ser Phe Lys
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<210> 21

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 21

Glu Met Asn Pro Pro Asp Asn Ile Lys
1 5

<210> 22

<211> 8

<212> PRT

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<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 22

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1 5

<210> 23

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

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Ser Val Pro Gly His Asp Asn Lys
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<210> 24

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 24

Met Gln Phe Glu Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu
1 5 10 15
Lys

<210> 25
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 25
Asp Leu Phe Lys
1

<210> 26
<211> 4
<212> PRT
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<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 26
Leu Ile Leu Lys
1

<210> 27
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 27
Glu Asp Glu Leu Gly Asp Arg
1 5

<210> 28
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18